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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/848,737	05/19/2004	Hsiang-Fu Kung	V9661.0080	7269

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EXAMINER	
MOSHER, MARY	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/848,737	KUNG ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5,6,10,12 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-9,11,13 and 15-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

T.D

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I, species SEQ ID NO:1 in the reply filed on June 7, 2005 is acknowledged. The traversal is on the ground(s) that (A) SEQs 1-6 all correspond to sequences within a single gene encoding the replicase, (B) the Commissioner's waiver permits search of up to 10 independent nucleotide sequences and nucleotide sequences encoding the same protein are not independent and distinct, and (C) that search of the different sequences is not unduly burdensome. This is not found persuasive because (A) the sequences corresponding to different regions of the replicase gene are related as subcombinations disclosed as usable together in a single combination. Subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, each of the short inhibitory RNA sequences can be used separately from each of the others. See MPEP § 806.05(d). (B) The Commissioner's waiver on what constitutes a "reasonable number for examination purposes" was based on the search burden in 1996; however, since that date, the amount of sequence information to be searched has doubled approximately every six months, so that the burden now is substantially greater. The different oligonucleotides do not encode the same protein, they differ in structure from each other by more than degenerate codons. (C) Search of the different sequences is unduly burdensome, because each targets a different region of the genome and mere search of the sequence is not sufficient for determination of patentability.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5, 6, 10, 12, 14, and parts of claims 15-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 7, 2005.

Claim Rejections - 35 USC § 112

Claims 1-4, 7-9, 11, 13, 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 18, and 19 are indefinite in reciting "a portion thereof" without limitation. Are the claims really meant to read on any nucleic acid sharing one or two bases with the recited sequence? This affects the dependent claims.

Claim 4 is indefinite for the following reason. Claim 1 is drawn to a nucleic acid comprising a particular sequence, and claim 4 is drawn to a nucleic acid which hybridizes to the nucleic acid of claim 1. If SEQ ID NO:1 were cloned into, say, plasmid pBR322 to make clone A, then clone A would comprise SEQ ID NO:1, and meet the limitations of claim 1. Unmodified pBR322 would hybridize to clone A, and therefore would meet the limitations of claim 4. This illustrates that claim 4 does not set any definite metes and bounds on the nucleic acids claimed.

It is noted for the record that the specification defines "hybridizes under stringent conditions" as meaning conditions where 70% identical sequences hybridize, see page 8.

In claims 7, 18, and 19, does "a complement thereof" mean the complement of the entire recited sequence, or does "a complemement" encompass shorter complementary sequences?

Claim 8 is drawn to "a host cell" containing a vector. Is the claim meant to be drawn to isolated host cells, or is the claim meant to encompass cells in an intact organism? If the latter is intended, is the intent also to claim organisms that transiently comprise the vector, and if that is the case, does possession of the organism revert to the original owner when the vector is eliminated? If an intact organism is intended, applicant is warned that the claim will be rejected as nonstatutory, since the claim would encompass a transgenic human.

Claims 9, 11, 13, 15-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method for inhibiting SARS infection or replication using SEQ ID NO:1, does not reasonably provide enablement for body-treating methods and compositions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification suggests a number of different uses for the claimed nucleic acid, specifically, as an siRNA to inhibit SARS infection and replication, as a nucleic acid immunogen, and as expression vector to produce the encoded protein. The specification shows that SEQ ID NO:1 is effective at reducing SARS infection and replication in cultured cells, but provides no evidence that the encoded oligopeptide induces a useful immune response or that the encoded protein reacts with antibodies

from virus-infected subjects. Since the encoded oligopeptide is part of the nonstructural gene, one skilled in the art would have reason to doubt an unsupported assertion that an immune response against this oligopeptide would prevent or treat infection, or that the peptide would be useful diagnostically. Considering the limited guidance, the unpredictability of a useful immune response, and the absence of working examples, it is concluded that undue experimentation would be required to use the claimed immunogenic formulations and kits. The specification also fails to teach how to use all of the "portions" and "complements" encompassed by the claims.

Furthermore, in regard to pharmaceutical compositions and methods, the specification fails to teach how to administer the nucleic acids in a manner to achieve the desired therapeutic result. Applicant's own publication on siRNAs states that "Their clinical usefulness, however, has yet to be demonstrated." (He et al, JAMA 290:2665-2666, 2003) The review by Paroo et al (Trends in Biotechnology 22:390-392, 2004) is cited as evidence that pharmaceutical use of siRNAs was not routine as of the date of the invention. Considering the state of the art, the limited teachings in the specification, and the absence of a working example, it is concluded that undue experimentation would be required to use the claimed pharmaceutical compositions and treatments.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention encompasses non-statutory subject matter. If "A host cell" includes intact organisms,

the claim reads upon transgenic humans, which constitute nonstatutory subject matter. This rejection could be obviated by amending the claim to recite "An isolated host cell."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4 are rejected under 35 U.S.C. 102(a) as being anticipated by Genbank locus AY274119, version AY27419.1 or GI:29826276. The Genbank sequence comprises a portion of SEQ ID NO:1 (all of SEQ ID NO: 1 except the terminal TT dinucleotide). See approximately nucleotides 760-780. The Genbank sequence is recited as a DNA, which would be double stranded; the "organism" information also states 'ssRNA positive-strand virus, no DNA stage," thereby teaching the RNA version of the same sequence. Therefore the reference meets each and every limitation of these claims. This Genbank entry was publicly available on April 14, 2003. Please note, the website "SARS-associated Coronavirus" is cited as evidence that similar sequence data was publicly available 2 days earlier.

Claims 1-4, 7-9, 11, 13, 15-19 are rejected under 35 U.S.C. 102(e) as being anticipated by McSwiggen et al WO 2004/092383. McSwiggen claims priority to 60/462,874, which describes the claimed invention prior to applicant's effective date. McSwiggen teaches a short interfering nucleic acid comprising any contiguous SARS sequence of about 19-25 contiguous bases, see e.g. page 12, lines 12-15. The reference also teaches addition of two 3' terminal deoxythymidine residues, see e.g. page 21, lines 18-28; vectors and host cells, see e.g. page 27, lines 19-23; pharmaceuticals and in vivo administration, see e.g. pages 110-123, 134-138. If the claimed nucleic acid is immunogenic, then the reference nucleic acid would inherently share the same characteristic. The reference also explicitly teaches double-stranded siRNAs which comprise a portion of SEQ ID NO:1, see Table II, page 147, the lines beginning with "759" and "777" (SEQ ID nos. 43, 44, 1694, 1695). Therefore the reference teaches each and every element of the invention as claimed.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Fodor et al US 2001/0053519. Fodor teaches the formation of an array which comprises every single 10-mer (see Example 2, beginning on page 12). This complete set of 10-mers necessarily and inherently comprises nucleic acids which constitute a portion of SEQ ID NO:1, and nucleic acids which hybridize under stringent conditions to SEQ ID NO:1.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

8/8/05

MARY E. MOSHER, PH.D.
PRIMARY EXAMINER